

WHAT IS CLAIMED IS:

1. A method for enhancing capacity of impaired bone marrow cells to promote development of collateral blood vessels in a patient in need, said method comprising:
growing the impaired bone marrow cells under suitable culture conditions in a suitable media for a period of time sufficient to promote production by the bone marrow cells of early attaching cells;
transfecting at least a portion of the early attaching cells with a vector comprising a polynucleotide that encodes one or more agents selected from angiogenic cytokines, growth factors and mammalian angiogenesis-promoting factors, and
culturing the transfected early attaching cells so as to allow production of the one or more agents,
thereby enhancing capacity of the impaired bone marrow cells and/or the media derived from these cells while being grown in culture to promote development of collateral blood vessels in the patient into which the cells and/or the media are delivered as compared with that of either non-transfected cells or media obtained from non-transfected cells grown in culture.
2. The method of claim 1, wherein the bone marrow cells are impaired by donor aging.
3. The method of claim 1, wherein the bone marrow cells are impaired by the donor having a disorder that impairs naturally occurring angiogenic processes found in normal young healthy individuals.
4. The method of claim 1, wherein the disorder is hypercholesterolemia.
5. The method of claim 1, wherein the donor is the patient.
6. The method of claim 1, wherein the cells are grown in culture for about 12 hours to about 12 days.
7. The method of claim 1, wherein the period of time is from about 12 hours to about 3 days.

8. The method of claim 1, further comprising obtaining bone marrow from a donor and filtering the bone marrow to obtain the bone marrow cells.
9. The method of claim 8, wherein the filtering removes particles larger than from about 300 μ to about 200 μ .
10. The method of claim 1, wherein the one or more agents are selected from hypoxia inducing factor-1 (HIF-1), endothelial PAS domain protein 1 (EPAS1), Monocyte Chemoattractant Protein 1 (MCP-1), granulocyte-monocyte colony stimulatory factor (GM-CSF), PR39, a fibroblast growth factor (FGF), and a nitric oxide synthase (NOS).
11. The method of claim 1, wherein the vector is selected from a plasmid vector and an adenoviral vector.
12. The method of claim 10, wherein the vector is an adenoviral vector.
13. The method of claim 12, wherein the agent is selected from PR39, a FGF and a NOS.
14. The method of claim 1, further comprising stimulating the transfected early attaching cells.
15. The method of claim 1, wherein the cells are marrow-derived stromal cells.
16. The method of claim 15, wherein the media is derived by culturing the marrow-derived stromal cells.

17. A method for enhancing collateral blood vessel formation in a patient in need thereof, said method comprising:

obtaining autologous bone marrow from the patient;

growing the autologous bone marrow under suitable culture conditions in a container for a period of time sufficient to promote production by the bone marrow of early attaching cells;

transfecting at least a portion of the early attaching cells with a vector comprising a polynucleotide that encodes one or more agents selected from a fibroblast growth factor (FGF), a NOS, and PR39 so as to cause expression of the one or more agents; and

directly administering to a desired site in the patient an effective amount of the transfected early attaching cells and/or media derived from the transfected cells while being grown in culture,

thereby enhancing collateral blood vessel formation at the site in the patient.

18. A method for enhancing collateral blood vessel formation in a patient in need thereof, said method comprising:

growing bone marrow under suitable culture conditions for a period of time sufficient to promote production by the bone marrow of early attaching cells;

transfecting at least a portion of the early attaching cells with a vector comprising a polynucleotide that encodes one or more agents selected from angiogenic cytokines, growth factors and mammalian angiogenesis-promoting factors for expression by the early attaching cells; and

culturing the transfected early attaching cells in a culture medium and for a time suitable to allow expression by the cells of the one or more agents, thereby producing conditioned medium; and

directly administering to a desired site in the patient an effective amount of the transfected early attaching cells and/or the conditioned medium,

thereby enhancing collateral blood vessel formation at the site in the patient.

19. The method of claim 18, wherein the early attaching cells are marrow-derived stromal cells and the cells are directly administered to a site of ischemia in the patient.

20. The method of claim 18, wherein the early attaching cells are marrow-derived stromal cells and the conditioned medium is directly administered to a site of ischemia in the patient.
21. The method of claim 18, wherein the cells and/or the conditioned medium are injected into the blood stream for administration to the site.
22. The method of claim 20, wherein the cells and/or the conditioned medium are injected into an artery supplying the site.
23. The method of claim 18, wherein the period of time is from about 3 hours to about 12 days.
24. The method of claim 23, wherein the period of time is from about 3 hours to about 3 days.
25. The method of claim 18, further comprising filtering the bone marrow prior to culturing of the bone marrow to obtain the early attaching cells.
26. The method of claim 25, wherein the bone marrow is autologous bone marrow.
27. The method of claim 18, wherein the agent is a transcription factor that promotes mammalian angiogenesis.
28. The method of claim 18, wherein the vector is an adenoviral vector.
29. The method of claim 28, wherein the agent is selected from a fibroblast growth factor (FGF), a NOS, and PR39 .
30. The method of claim 29, wherein the agent is selected from FGF-1, FGF-2, FGF-4, and FGF-5.
31. The method of claim 29, wherein the agent is selected from inducible NOS and endothelial NOS.

32. The method of claim 29, wherein the agent is PR39.
33. The method of claim 18, wherein the transfected cells are injected directly into heart or leg muscle to promote angiogenesis therein.
34. The method of claim 18, wherein the method enhances collateral blood vessel formation in the heart or leg muscle.
35. The method of claim 18, wherein the method promotes development of newly implanted myocardial cells.
36. The method of claim 18, wherein the method promotes electrical conductivity of the heart of a patient with cardiac electrical pathway impairment.
37. The method of claim 18, wherein the method enhances myocardial function in a patient with impaired myocardial function.
38. The method of claim 18, wherein the method treats a left or right ventricular condition causing impaired heart function in the heart of the patient.
39. A therapeutic composition comprising early attaching cells derived from bone marrow, which cells have been transfected with a vector comprising a polynucleotide that encodes one or more agents selected from angiogenic cytokines growth factors, and angiogenesis-promoting factors.
40. The therapeutic composition of claim 39, further comprising conditioned medium in which the cells have been grown in culture for a time sufficient to allow expression of one or more of the agents.
41. The composition of claim 39, wherein the polynucleotide further comprises a transcription regulatory region operatively associated with the polynucleotide.

42. The composition of claim 39, wherein the transfected cells have been stimulated by exposure to hypoxia.
43. The composition of claim 39, further comprising heparin or another anticoagulent.
44. The composition of claim 39, wherein the vector is an adenoviral vector.
45. The composition of claim 39, wherein the early attaching cells are marrow-derived stromal cells.
46. The composition of claim 39, wherein the composition is intended to be injected into a patient having ischemic tissue and the early attaching cells are derived from bone marrow obtained from the patient.